

WHAT IS CLAIMED IS:

1. A purified or isolated nucleic acid sequence consisting essentially of one the sequence of nucleotides of SEQ ID NOs: 1-93, wherein expression of said nucleic acid in a microorganism is capable of inhibiting proliferation of a microorganism.
- 5 2. The nucleic acid sequence of Claim 1, wherein said nucleic acid sequence is complementary to at least a portion of the nucleotide sequence of the coding strand of a gene whose expression is required for proliferation of a microorganism.
3. The nucleic acid of Claim 1, wherein said nucleic acid sequence has a nucleotide sequence complementary to at least a portion of the nucleotide sequence of an RNA required for proliferation of a microorganism.
- 10 4. The nucleic acid of Claim 3, wherein the nucleotide sequence of said RNA encodes more than one gene product.
5. A purified or isolated nucleic acid comprising a fragment of one of the nucleotide sequence of SEQ ID NOs: 1-93, said fragment selected from the group consisting of fragments comprising at least 10, at least 20, at least 25, at least 30, at least 50 and more than 50 consecutive nucleotides of one of the nucleotide sequences of SEQ ID NOs: 1-93.
- 15 6. A vector comprising a promoter operably linked to the nucleic acid sequence of Claims 1,2,3,4, or 5.
- 20 7. The vector of Claim 6, wherein said promoter is active in a microorganism selected from the group consisting of *Aspergillus fumigatus*, *Bacillus anthracis*, *Burkholderia cepacia*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*),
- 25 *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium botulinum*, *Clostridium difficile*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Klebsiella pneumoniae*, *Listeria monocytogenes*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Neisseria gonorrhoeae*, *Pseudomonas aeruginosa*,
- 30 *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Listeria monocytogenes*, *Moxarella catarrhalis*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella*

flexneri, *Shigella sonnei*, *Pseudomonas aeruginosa*, *Staphylococcus epidermidis*, *Streptococcus pneumoniae*, *Treponema pallidum*, *Yersinia pestis* and any species falling within the genera of any of the above species.

8. A host cell containing the vector of Claim 6.

5 ~~9.~~ A purified or isolated nucleic acid consisting essentially of the coding sequence of one of SEQ ID NOs: 106-112, 119-122, 134-160, 164-171, 179-265, 271-273, 275, and 279-286.

10 10. A fragment of the nucleic acid of Claim 8, said fragment comprising at least 10, at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive nucleotides of one of SEQ ID NOs: 106-112, 119-122, 134-160, 164-171, 179-265, 271-273, 275, and 279-286.

11. A vector comprising a promoter operably linked to the nucleic acid of Claim 9 or Claim 10.

15 ~~12.~~ A purified or isolated antisense nucleic acid comprising a nucleic acid sequence complementary to at least a portion of an intragenic sequence, intergenic sequence, sequences spanning at least a portion of two or more genes, 5' noncoding region, or 3' noncoding region within an operon comprising a proliferation-required gene whose activity or expression is inhibited by an antisense nucleic acid comprising one of SEQ ID NOs.: 1-93.

20 ~~13.~~ A purified or isolated nucleic acid comprising a nucleic acid having at least 70% identity to a sequence selected from the group consisting of SEQ ID NOs.: 1-93, fragments comprising at least 25 consecutive nucleotides of SEQ ID NOs.: 1-93, the sequences complementary to SEQ ID NOs.: 1-93 and the sequences complementary to fragments comprising at least 25 consecutive nucleotides of SEQ ID NOs.: 1-93 as
25 determined using BLASTN version 2.0 with the default parameters.

30 14. The nucleic acid of Claim 13, wherein said nucleic acid is from an organism selected from the group consisting of *Aspergillus fumigatus*, *Bacillus anthracis*, *Burkholderia cepacia*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium botulinum*, *Clostridium difficile*, *Cryptococcus neoformans*, *Enterobacter cloacae*,

Enterococcus faecalis, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*,
Klebsiella pneumoniae, *Listeria monocytogenes*, *Mycobacterium leprae*,
Mycobacterium tuberculosis, *Neisseria gonorrhoeae*, *Pseudomonas aeruginosa*,
Salmonella choleraesuis, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*,
5 *Salmonella typhimurium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Listeria*
monocytogenes, *Moxarella catarrhalis*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella*
flexneri, *Shigella sonnei*, *Pseudomonas aeruginosa*, *Staphylococcus epidermidis*,
Streptococcus pneumoniae, *Treponema pallidum*, *Yersinia pestis* and any species falling
within the genera of any of the above species.

10 ~~15.~~ A vector comprising a promoter operably linked to a nucleic acid
encoding a polypeptide whose expression is inhibited by an antisense nucleic acid
comprising one of SEQ ID NOs.: 1-93.

16. A host cell containing the vector of Claim 15.

15 17. The vector of Claim 15, wherein said polypeptide comprises a
polypeptide comprising a sequence selected from the group consisting of SEQ ID NOs:
299-305, 312-315, 327-353, 357-364, 372-458, 464-466, 468 and 472-479.

20 ~~18.~~ A purified or isolated polypeptide comprising a polypeptide whose
expression is inhibited by an antisense nucleic acid comprising one of SEQ ID NOs.: 1-
93, or a fragment selected from the group consisting of fragments comprising at least 5,
at least 10, at least 20, at least 30, at least 40, at least 50, at least 60 or more than 60
consecutive amino acids of one of the said polypeptides.

25 19. The polypeptide of Claim 18, wherein said polypeptide comprises a
polypeptide comprising one of SEQ ID NOs.: 299-305, 312-315, 327-353, 357-364,
372-458, 464-466, 468 and 472-479 or a fragment comprising at least 5, at least 10, at
least 20, at least 30, at least 40, at least 50, at least 60 or more than 60 consecutive
amino acids of a polypeptide comprising a sequence selected from the group consisting
of SEQ ID NOs.: 299-305, 312-315, 327-353, 357-364, 372-458, 464-466, 468 and
472-479.

30 ~~20.~~ A purified or isolated polypeptide comprising a polypeptide having at
least 25% identity to a polypeptide whose expression is inhibited by a sequence selected
from the group consisting of SEQ ID NOs.: 1-93, or at least 25% identity to a fragment
comprising at least 5, at least 10, at least 20, at least 30, at least 40, at least 50, at least

60 or more than 60 consecutive amino acids of a polypeptide whose expression is inhibited by a nucleic acid selected from the group consisting of SEQ ID NOs.: 1-93 as determined using FASTA version 3.0t78 with the default parameters.

21. The polypeptide of Claim 20, wherein said polypeptide has at least 25% identity to a polypeptide comprising one of SEQ ID NOs: 299-305, 312-315, 327-353, 357-364, 372-458, 464-466, 468 and 472-479 or at least 25% identity to a fragment comprising at least 5, at least 10, at least 20, at least 30, at least 40, at least 50, at least 60 or more than 60 consecutive amino acids of a polypeptide comprising one of SEQ ID NOs.: 299-305, 312-315, 327-353, 357-364, 372-458, 464-466, 468 and 472-479 as determined using FASTA version 3.0t78 with the default parameters.

22. An antibody capable of specifically binding the polypeptide of one of Claims 18-21.

~~23.~~ A method of producing a polypeptide, comprising introducing a vector comprising a promoter operably linked to a nucleic acid encoding a polypeptide whose expression is inhibited by an antisense nucleic acid comprising one of SEQ ID NOs.: 1-93 into a cell and expressing said polypeptide.

24. The method of Claim 23, further comprising the step of isolating said polypeptide.

25. The method of Claim 23, wherein said polypeptide comprises a sequence selected from the group consisting of SEQ ID NOs.: 299-305, 312-315, 327-353, 357-364, 372-458, 464-466, 468 and 472-479.

~~26.~~ A method of inhibiting proliferation of a microorganism comprising inhibiting the activity or reducing the amount of a gene product whose expression is inhibited by an antisense nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs.: 1-93 or inhibiting the activity or reducing the amount of a nucleic acid encoding said gene product.

27. The method of Claim 26, wherein said gene product comprises a polypeptide comprising a sequence selected from the group consisting of SEQ ID NOs.: 299-305, 312-315, 327-353, 357-364, 372-458, 464-466, 468 and 472-479.

~~28.~~ A method for identifying a compound which influences the activity of a gene product required for proliferation, said gene product comprising a gene product

whose expression is inhibited by an antisense nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs.: 1-93, said method comprising:

contacting said gene product with a candidate compound; and
determining whether said compound influences the activity of said gene product.

29. The method of Claim 28, wherein said gene product is a polypeptide and said activity is an enzymatic activity.

30. The method of Claim 28, wherein said gene product is a polypeptide and said activity is a carbon compound catabolism activity.

31. The method of Claim 28, wherein said gene product is a polypeptide and said activity is a biosynthetic activity.

32. The method of Claim 28, wherein said gene product is a polypeptide and said activity is a transporter activity.

33. The method of Claim 28, wherein said gene product is a polypeptide and said activity is a transcriptional activity.

34. The method of Claim 28, wherein said gene product is a polypeptide and said activity is a DNA replication activity.

35. The method of Claim 28, wherein said gene product is a polypeptide and said activity is a cell division activity.

36. A compound identified using the method of Claim 28.

37. The method of Claim 28, wherein said gene product is a polypeptide comprising a sequence selected from the group consisting of SEQ ID NOs.: 299-305, 312-315, 327-353, 357-364, 372-458, 464-466, 468 and 472-479.

~~38.~~ A method for identifying a compound or nucleic acid having the ability to reduce the activity or level of a gene product required for proliferation, said gene product comprising a gene product whose activity or expression is inhibited by an antisense nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs.: 1-93, said method comprising:

(a) providing a target that is a gene or RNA, wherein said target comprises a nucleic acid encoding said gene product;

(b) contacting said target with a candidate compound or nucleic acid;
and

(c) measuring an activity of said target.

39. The method of Claim 38, wherein said target is a messenger RNA molecule and said activity is translation of said messenger RNA.

40. The method of Claim 38, wherein said target is a messenger RNA molecule and said activity is transcription of a gene encoding said messenger RNA.

41. The method of Claim 38, wherein said target is a gene and said activity is transcription of said gene.

42. The method of Claim 38, wherein said target is a nontranslated RNA and said activity is processing or folding of said nontranslated RNA or assembly of said nontranslated RNA into a protein/RNA complex.

43. The method of Claim 38, wherein said target gene or RNA encodes a polypeptide comprising a sequence selected from the group consisting of SEQ ID NOs.: 299-305, 312-315, 327-353, 357-364, 372-458, 464-466, 468 and 472-479.

44. A compound or nucleic acid identified using the method of Claim 38.

45. A method for identifying a compound which reduces the activity or level of a gene product required for proliferation of a microorganism, wherein the activity or expression of said gene product is inhibited by an antisense nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs.: 1-93, said method comprising the steps of:

(a) expressing a sub-lethal level of an antisense nucleic acid complementary to a nucleic acid encoding said gene product in a cell to reduce the activity or amount of said gene product in said cell, thereby producing a sensitized cell;

(b) contacting said sensitized cell with a compound; and

(c) determining whether said compound inhibits the growth of said sensitized cell.

46. The method of Claim 45, wherein said determining step comprises determining whether said compound inhibits the growth of said sensitized cell to a greater extent than said compound inhibits the growth of a nonsensitized cell.

47. The method of Claim 45, wherein said cell is selected from the group consisting of bacterial cells, fungal cells, plant cells, and animal cells.

48. The method of Claim 45, wherein said cell is a Gram negative bacterium.

49. The method of Claim 45, wherein said cell is an *E. coli* cell.

50. The method of Claim 45, wherein said cell is from an organism selected from the group consisting of *Aspergillus fumigatus*, *Bacillus anthracis*, *Burkholderia cepacia*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called
5 *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium botulinum*, *Clostridium difficile*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*,
10 *Klebsiella pneumoniae*, *Listeria monocytogenes*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Neisseria gonorrhoeae*, *Pseudomonas aeruginosa*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Listeria monocytogenes*, *Moxarella catarrhalis*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Pseudomonas aeruginosa*, *Staphylococcus epidermidis*,
15 *Streptococcus pneumoniae*, *Treponema pallidum*, *Yersinia pestis* and any species falling within the genera of any of the above species.

51. The method of Claim 45, wherein said antisense nucleic acid is transcribed from an inducible promoter.

20 52. The method of Claim 51, further comprising the step of contacting said cell with a concentration of inducer which induces said antisense nucleic acid to a sub-lethal level.

53. The method of Claim 45, wherein growth inhibition is measured by monitoring optical density of a culture growth solution.

25 54. The method of Claim 45, wherein said gene product is a polypeptide.

Sub 13 55. The method of Claim 54, wherein said polypeptide comprises a sequence selected from the group consisting of SEQ ID NOs.: 299-305, 312-315, 327-353, 357-364, 372-458, 464-466, 468 and 472-479.

56. The method of Claim 45, wherein said gene product is an RNA.

30 57. A compound identified using the method of Claim 45.

~~58.~~ A method for inhibiting cellular proliferation comprising introducing a compound with activity against a gene whose activity or expression is inhibited by an

antisense nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs.: 1-93 or a compound with activity against the product of said gene into a population of cells expressing said gene.

5 59. The method of Claim 58, wherein said compound is an antisense nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs.: 1-93, or a proliferation-inhibiting portion thereof.

10 60. The method of Claim 59, wherein said proliferation inhibiting portion of one of SEQ ID NOs.: 1-93 is a fragment comprising at least 10, at least 20, at least 25, at least 30, at least 50 or more than 51 consecutive nucleotides of one of SEQ ID NOs.: 1-93.

61. The method of Claim 58, wherein said population is a population selected from the group consisting of bacterial cells, fungal cells, plant cells, and animal cells.

15 62. The method of Claim 58, wherein said population is a population of Gram negative bacteria.

63. The method of Claim 58, wherein said population is a population of *E. coli* cells.

20 64. The method of Claim 58, wherein said population is a population selected from the group consisting of *Aspergillus fumigatus*, *Bacillus anthracis*, *Burkholderia cepacia*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium botulinum*, *Clostridium difficile*, *Cryptococcus neoformans*, *Enterobacter cloacae*,
25 *Enterococcus faecalis*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Klebsiella pneumoniae*, *Listeria monocytogenes*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Neisseria gonorrhoeae*, *Pseudomonas aeruginosa*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Listeria monocytogenes*,
30 *Moxarella catarrhalis*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Pseudomonas aeruginosa*, *Staphylococcus epidermidis*,

Streptococcus pneumoniae, *Treponema pallidum*, *Yersinia pestis* and any species falling within the genera of any of the above species.

65. The method of Claim 58, wherein said gene encodes a polypeptide comprising a sequence selected from the group consisting of SEQ ID NOs.: 299-305, 312-315, 327-353, 357-364, 372-458, 464-466, 468 and 472-479.

~~66.~~ A preparation comprising an effective concentration of an antisense nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs.: 1-93, or a proliferation-inhibiting portion thereof in a pharmaceutically acceptable carrier.

67. The preparation of Claim 66, wherein said proliferation-inhibiting portion of one of SEQ ID NOs.: 1-93 comprises at least 10, at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive nucleotides of one of SEQ ID NOs.: 1-93.

~~68.~~ A method for inhibiting the activity or expression of a gene in an operon required for proliferation wherein the activity or expression of at least one gene in said operon is inhibited by an antisense nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs.: 1-93, said method comprising contacting a cell in a cell population with an antisense nucleic acid comprising at least a proliferation-inhibiting portion of said operon.

69. The method of Claim 68, wherein said antisense nucleic acid comprises a sequence selected from the group consisting of SEQ ID NOs.: 1-93 or a proliferation inhibiting portion thereof.

70. The method of Claim 68, wherein said cell is contacted with said antisense nucleic acid by introducing a plasmid which expresses said antisense nucleic acid into said cell population.

71. The method of Claim 68, wherein said cell is contacted with said antisense nucleic acid by introducing a phage which expresses said antisense nucleic acid into said cell population.

72. The method of Claim 68, wherein said cell is contacted with said antisense nucleic acid by expressing said antisense nucleic acid from the chromosome of cells in said cell population.

73. The method of Claim 68, wherein said cell is contacted with said antisense nucleic acid by introducing a promoter adjacent to a chromosomal copy of said antisense nucleic acid such that said promoter directs the synthesis of said antisense nucleic acid.

5 74. The method of Claim 68, wherein said cell is contacted with said antisense nucleic acid by introducing a retron which expresses said antisense nucleic acid into said cell population.

75. The method of Claim 68, wherein said cell is contacted with said antisense nucleic acid by introducing a ribozyme into said cell-population, wherein a binding portion of said ribozyme is complementary to said antisense oligonucleotide.

76. The method of Claim 68, wherein said cell is contacted with said antisense nucleic acid by introducing a liposome comprising said antisense oligonucleotide into said cell.

77. The method of Claim 68, wherein said cell is contacted with said antisense nucleic acid by electroporation of said antisense nucleic acid.

78. The method of Claim 68, wherein said antisense nucleic acid is a fragment comprising at least 10, at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive nucleotides of one of SEQ ID NOs.: 1-93.

79. The method of Claim 68 wherein said antisense nucleic acid is an oligonucleotide.

~~80.~~ A method for identifying a gene which is required for proliferation of a microorganism comprising:

(a) contacting a microorganism other than *E. coli* with a nucleic acid selected from the group consisting of SEQ ID NOs.: 1-93;

(b) determining whether said nucleic acid inhibits proliferation of said microorganism; and

(c) identifying the gene in said microorganism which is inhibited by said nucleic acid.

81. The method of Claim 80, wherein said microorganism is a Gram negative bacterium.

82. The method of Claim 80 wherein said microorganism is selected from the group consisting of *Aspergillus fumigatus*, *Bacillus anthracis*, *Burkholderia cepacia*,

Campylobacter jejuni, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium botulinum*, *Clostridium difficile*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Klebsiella pneumoniae*, *Listeria monocytogenes*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Neisseria gonorrhoeae*, *Pseudomonas aeruginosa*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Listeria monocytogenes*, *Moxarella catarrhalis*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Pseudomonas aeruginosa*, *Staphylococcus epidermidis*, *Streptococcus pneumoniae*, *Treponema pallidum*, *Yersinia pestis* and any species falling within the genera of any of the above species.

83. The method of Claim 80, further comprising introducing said nucleic acid into a vector functional in said microorganism prior to introducing said inhibitory nucleic acid into said microorganism.

~~84.~~ A method for identifying a compound having the ability to inhibit proliferation of a microorganism comprising:

(a) identifying in a first microorganism a homolog of a gene or gene product present in a second microorganism which is different than said first microorganism, wherein the activity or level of said gene or gene product is inhibited by a nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs. 1-93 ;

(b) identifying an inhibitory nucleic acid sequence which inhibits the activity of said homolog in said first microorganism;

(c) contacting said first microorganism with a sub-lethal level of said inhibitory nucleic acid, thus sensitizing said first microorganism;

(d) contacting the sensitized microorganism of step (c) with a compound; and

(e) determining whether said compound inhibits proliferation of said sensitized microorganism.

85. The method of Claim 84, wherein said determining step comprises determining whether said compound inhibits proliferation of said sensitized microorganism to a greater extent than said compound inhibits proliferation of a nonsensitized microorganism.

5 86. The method of Claim 84 wherein step (a) comprises identifying a homologous nucleic acid to a gene or gene product whose activity or level is inhibited by a nucleic acid selected from the group consisting of SEQ ID NOs. 1-93 or a nucleic acid encoding a homologous polypeptide to a polypeptide whose activity or level is inhibited by a nucleic acid selected from the group consisting of SEQ ID NOs. 1-93 by
10 using an algorithm selected from the group consisting of BLASTN version 2.0 with the default parameters and FASTA version 3.0t78 algorithm with the default parameters to identify said homologous nucleic acid or said nucleic acid encoding a homologous polypeptide in a database.

15 87. The method of Claim 84 wherein said step (a) comprises identifying a homologous nucleic acid or a nucleic acid encoding a homologous polypeptide by identifying nucleic acids which hybridize to said first gene.

88. The method of Claim 84 wherein the step (a) comprises expressing a nucleic acid selected from the group consisting of SEQ ID NOs. 1-93 in said microorganism.

20 89. The method of Claim 84, wherein said inhibitory nucleic acid is an antisense nucleic acid.

90. The method of Claim 84, wherein said inhibitory nucleic acid comprises an antisense nucleic acid to a portion of said homolog.

25 91. The method of Claim 84, wherein said inhibitory nucleic acid comprises an antisense nucleic acid to a portion of the operon encoding said homolog.

92. The method of Claim 84, wherein the step of contacting the first microorganism with a sub-lethal level of said inhibitory nucleic acid comprises directly contacting said microorganism with said inhibitory nucleic acid.

30 93. The method of Claim 84, wherein the step of contacting the first microorganism with a sub-lethal level of said inhibitory nucleic acid comprises expressing an antisense nucleic acid to said homolog in said microorganism.

94. The method of Claim 84, wherein said gene product comprises a polypeptide comprising a sequence selected from the group consisting of SEQ ID NOs.: 299-305, 312-315, 327-353, 357-364, 372-458, 464-466, 468 and 472-479.

95. A compound identified using the method of Claim 84.

5 ~~96.~~ A method of identifying a compound having the ability to inhibit proliferation comprising:

10 (a) contacting a microorganism other than *E. coli* with a sub-lethal level of a nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs. 1-93 or a portion thereof which inhibits the proliferation of *E. coli*, thus sensitizing said microorganism;

 (b) contacting the sensitized microorganism of step (a) with a compound; and

15 (c) determining whether said compound inhibits proliferation of said sensitized microorganism.

97. The method of Claim 96, wherein said determining step comprises determining whether said compound inhibits proliferation of said sensitized microorganism to a greater extent than said compound inhibits proliferation of a nonsensitized microorganism.

98. A compound identified using the method of Claim 96.

20 ~~99.~~ A method for identifying a compound having activity against a biological pathway required for proliferation comprising:

25 (a) sensitizing a cell by expressing a sub-lethal level of an antisense nucleic acid complementary to a nucleic acid encoding a gene product required for proliferation, wherein the activity or expression of said gene product is inhibited by an antisense nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs.: 1-93, in said cell to reduce the activity or amount of said gene product;

 (b) contacting the sensitized cell with a compound; and

30 (c) determining whether said compound inhibits the growth of said sensitized cell.

100. The method of Claim 99, wherein said determining step comprises determining whether said compound inhibits the growth of said sensitized cell to a greater extent than said compound inhibits the growth of a nonsensitized cell.

101. The method of Claim 99, wherein said cell is selected from the group consisting of bacterial cells, fungal cells, plant cells, and animal cells.

102. The method of Claim 99, wherein said cell is a Gram negative bacterium.

103. The method of Claim 99, wherein said Gram negative bacterium is *E. coli*.

104. The method of Claim 99, wherein said cell is selected from the group consisting of *Aspergillus fumigatus*, *Bacillus anthracis*, *Burkholderia cepacia*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium botulinum*, *Clostridium difficile*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Klebsiella pneumoniae*, *Listeria monocytogenes*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Neisseria gonorrhoeae*, *Pseudomonas aeruginosa*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Listeria monocytogenes*, *Moxarella catarrhalis*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Pseudomonas aeruginosa*, *Staphylococcus epidermidis*, *Streptococcus pneumoniae*, *Treponema pallidum*, *Yersinia pestis* and any species falling within the genera of any of the above species.

105. The method of Claim 99, wherein said antisense nucleic acid is transcribed from an inducible promoter.

106. The method of Claim 99, further comprising contacting the cell with an agent which induces expression of said antisense nucleic acid from said inducible promoter, wherein said antisense nucleic acid is expressed at a sub-lethal level.

107. The method of Claim 99, wherein inhibition of proliferation is measured by monitoring the optical density of a liquid culture.

108. The method of Claim 99, wherein said gene product comprises a polypeptide comprising a sequence selected from the group consisting of SEQ ID NOs.: 299-305, 312-315, 327-353, 357-364, 372-458, 464-466, 468 and 472-479

109. A compound identified using the method of Claim 99.

5 ~~110.~~ A method for identifying a compound having the ability to inhibit cellular proliferation comprising:

10 (a) contacting a cell with an agent which reduces the activity or level of a gene product required for proliferation of said cell, wherein said gene product is a gene product whose activity or expression is inhibited by an antisense nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs.: 1-93;

 (b) contacting said cell with a compound; and

 (c) determining whether said compound reduces proliferation of said contacted cell.

15 111. The method of Claim 110, wherein said determining step comprises determining whether said compound reduces proliferation of said contacted cell to a greater extent than said compound reduces proliferation of cells which have not been contacted with said agent.

20 112. The method of Claim 110, wherein said agent which reduces the activity or level of a gene product required for proliferation of said cell comprises an antisense nucleic acid to a gene or operon required for proliferation.

 113. The method of Claim 110, wherein said agent which reduces the activity or level of a gene product required for proliferation of said cell comprises a compound known to inhibit growth or proliferation of a microorganism.

25 114. The method of Claim 110, wherein said cell contains a mutation which reduces the activity or level of said gene product required for proliferation of said cell.

 115. The method of Claim 114, wherein said mutation is a temperature sensitive mutation.

30 116. The method of Claim 110, wherein said gene product comprises a polypeptide comprising a sequence selected from the group consisting of SEQ ID NOs.: 299-305, 312-315, 327-353, 357-364, 372-458, 464-466, 468 and 472-479

 117. A compound identified using the method of Claim 110.

118. A method for identifying the biological pathway in which a proliferation-required gene or its gene product lies, wherein said gene or gene product comprises a gene or gene product whose activity or expression is inhibited by an antisense nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs.: 1-93, said method comprising:

- (a) expressing a sub-lethal level of an antisense nucleic acid which inhibits the activity of said proliferation-required gene or gene product in a cell;
- (b) contacting said cell with a compound known to inhibit growth or proliferation of a microorganism, wherein the biological pathway on which said compound acts is known; and
- (c) determining whether said cell is sensitive to said compound.

119. The method of Claim 118, wherein said determining step comprises determining whether said cell has a substantially greater sensitivity to said compound than a cell which does not express said sub-lethal level of said antisense nucleic acid and wherein said gene or gene product lies in the same pathway on which said compound acts if said cell expressing said sub-lethal level of said antisense nucleic acid has a substantially greater sensitivity to said compound than said cell which does not express said sub-lethal level of said antisense nucleic acid.

120. The method of Claim 118, wherein said gene product comprises a polypeptide comprising a sequence selected from the group consisting of SEQ ID NOs.: 299-305, 312-315, 327-353, 357-364, 372-458, 464-466, 468 and 472-479

121. A method for determining the biological pathway on which a test compound acts comprising:

- (a) expressing a sub-lethal level of an antisense nucleic acid complementary to a proliferation-required nucleic acid in a cell, wherein the activity or expression of said proliferation-required nucleic acid is inhibited by an antisense nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs.: 1-93 and wherein the biological pathway in which said proliferation-required nucleic acid or a protein encoded by said proliferation-required polypeptide lies is known,
- (b) contacting said cell with said test compound; and
- (c) determining whether said cell is sensitive to said test compound.

122. The method of Claim 121, wherein said determining step comprises determining whether said cell has a substantially greater sensitivity to said test compound than a cell which does not express said sub-lethal level of said antisense nucleic acid.

5 123. The method of Claim 121, further comprising:

(d) expressing a sub-lethal level of a second antisense nucleic acid complementary to a second proliferation-required nucleic acid in a second cell, wherein said second proliferation-required nucleic acid is in a different biological pathway than said proliferation-required nucleic acid in step (a); and

10 (e) determining whether said second cell does not have a substantially greater sensitivity to said test compound than a cell which does not express said sub-lethal level of said second antisense nucleic acid, wherein said test compound is specific for the biological pathway against which the antisense nucleic acid of step (a) acts if said second cell does not have substantially greater sensitivity to said test compound.

15 ~~124.~~ A purified or isolated nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs.: 1-93.

~~125.~~ A compound which interacts with a gene or gene product whose activity or expression is inhibited by an antisense nucleic acid comprising one of SEQ ID NOs.: 1-93 to inhibit proliferation.

20 ~~126.~~ A compound which interacts with a polypeptide whose expression is inhibited by an antisense nucleic acid comprising one of SEQ ID NOs.: 1-93 to inhibit proliferation.

~~127.~~ A method for manufacturing an antibiotic comprising the steps of:
25 screening one or more candidate compounds to identify a compound that reduces the activity or level of a gene product required for proliferation, said gene product comprising a gene product whose activity or expression is inhibited by an antisense nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs.: 1-93; and

30 manufacturing the compound so identified.

Sub A4 128. The method of Claim 127, wherein said screening step comprises performing any one of the methods of Claims 28, 38, 45, 96, 99 and 110.

129. A method for inhibiting proliferation of a microorganism in a subject comprising administering a compound that reduces the activity or level of a gene product required for proliferation of said microorganism, said gene product comprising a gene product whose activity or expression is inhibited by an antisense nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs.: 1-93 to said subject.

130. The method of Claim 129 wherein said subject is selected from the group consisting of vertebrates, mammals, avians, and human beings.

131. The method of Claim 129, wherein said gene product comprises a polypeptide comprising a sequence selected from the group consisting of SEQ ID NOs.: 299-305, 312-315, 327-353, 357-364, 372-458, 464-466, 468 and 472-479.

Add A5